REMARKS

Claims 1-12 and 14-28 are pending in the current application. In an office action dated March 21, 2007 ("Office Action"), the Examiner rejected claims 1-2, 4, 7-8, 10-12, and 14-15, 17, and 28 under 35 U.S.C. § 103(a) as being unpatentable over Larson et al., "Calculus with Analytic Geometry, 1990, D.C. Heath and Company; Lexington, Massachusetts; Section 14.1, pages 785-795" ("Larson") in view of Schadt et al., Journal of Cellular Biochemistry Supplement 37:120-125, 2001 ("Schadt"), rejected claims 20-21, 23, and 26-27 under 35 U.S.C. § 103(a) as being unpatentable over Larson in view of Schadt and further in view of a website:
http://web.archive.org/web/20021008184825/http://www.s2.chalmers.se/~agrell/hpercues ("Chalmers"). Applicants' representative respectfully traverses the 35 U.S.C. § 103(a) rejections of claims 1-12 and 14-28.

Applicants' representative confesses to being bewildered by the continued reliance on Larson by the Examiner. In a previously filed response, Applicants' representative provided very clear statements with regard the inapplicability of this reference to currently claimed invention. The form and content of the current rejections do not come close to meeting the requirements of a *prima facie* case of obviousness. For example, as discussed in MPEP § 2142, to establish a prima facie case of obviousness, "the *prior art reference* (or references when combined) *must teach or suggest* all of the claim limitations" (emphasis added). A *prima facie* case for obviousness is not made by reading claim language onto unrelated figures from a textbook chapter concerning unrelated mathematical subjects, which neither teaches, suggests, nor mentions the claimed subject matter nor even uses the terms and phrases employed in the claim.

Consider, as an example, claim 1, provided below for the Examiner's convenience:

> 1. A method for selecting a set of normalizing data points from *n* data sets, where *n* is at least 3, containing data points having values and identities, the method comprising:
>
> receiving *n* data sets;
>
> considering the data points to be distributed in an *n*-dimensional data-point space;

determining one or more order-preserving sequences of data points within the *n*-dimensional data-point space,

selecting, as normalizing data points, data points from the one or more order-preserving sequences; and

storing the selected normalizing points in a computer memory as a basis for subsequent normalization of the *n* data sets.

Please next consider the elements of claim 1. The first element is directed to "receiving *n* data sets." Applicants' representative cannot find a single instance of the word "data" or the phrase "data set" in Larson, nor can Applicants' representative find any teaching, mention, or suggestion of "receiving a data set" in Larson. Claim 1 clearly defines a data set as "containing data points having values and identities." Furthermore, the definition is consistent with the definitions and uses of the phrases "data point" and "data set" in the current application, for example beginning on line 3 of page 17:

> Data points, or features, in a number of microarray data sets have both identities and values. The values of a data point are generally a measure of scanned intensities of light or radiation emitted from labeled target molecules bound to the feature, and the identity may be two-coordinate indexes, a sequence number, or an alphanumeric label that uniquely identifies the feature within the data set. A data point may also, in certain cases, be associated with a weight, where the weight expresses a measure of confidence, constancy, or some other parameter or characteristic.
>
> An order-preserving sequence is a sequence of data points in which the values of the data points within the sequence uniformly increase within the sequence. When a sequence is defined as an ordered subset of points within a data set, then a longest-order-preserving sequence ("LOPS") is the maximally sized, one or more ordered subsets of points selected from the data set that are ordered by signal strength or by some other associated value, parameter, or characteristic. A heaviest-order-preserving sequence ("HOPS") is the order-preserving sequence with greatest sums of weights associated with data points in order-preserving sequence.

Larson does not use the phrases "data point" and "data set" because Larson is not concerned with data points or data sets. Instead, Larson is concerned with solid analytic geometry and vectors in space. Geometry is concerned with geometrical points, but geometrical points are simply locations, generally specified as ordered sets of coordinates with respect to an arbitrarily defined set of axes. The identity of a geometrical point is its location. Geometrical points have no size, shape, or other distinguishing values or

features. It is therefore neither surprising nor coincidental that Larson does not discuss values associated with geometric points. Beginning on line 23 of page 17 of the current application, a 2-dimensional representation of two data sets is described:

> Figures 10A-D illustrate the two-dimensional LOPS. In Figure 10A, a number of data points, such as data point 1002, are distributed in a two-dimensional space defined by an orthogonal coordinate system. The positive, horizontal axis 1004 corresponds to a first coordinate x, and the vertical axis 1006 in Figure 10A is the positive axis for the coordinate y. Each data point, such as data point 1002, has an identity as well as an x value and a y value represented by the position of the data point within the two-dimensional space. Commonly, the data points are associated with Cartesian coordinates (x, y) where x is the value of the data point with respect to the x axis, and y is the value of the data point with respect to the y axis. Such a two-dimensional distribution may arise from scanning a microarray at two different frequencies, with the x values representing signal intensities scanned at one frequency, and the y values representing signal intensities scanned at another frequency.

Each data point is associated with two signal-intensity values, one intensity value in a first data set, and the other intensity value in the second data set, as well as an identity. The identity of a data point is a name or number identifying the feature in all n data sets. For example, the identity of a data point may be the name of genetic locus including a sequence complementary to the probe included in a particular feature of a microarray, and the values of the data point in n data sets are the intensity values measured at that feature in n experiments. Larson does not teach, mention, or suggest anything whatsoever to do with data sets and data points. The phrase "data set," in the scientific community, is used to refer to observations collected by experimental procedures. Geometric points are not data, but are, instead, arbitrarily *defined* locations in space. Geometric points are the product of definition, rather than observation. Again, the teaching must be found in the reference. Redefining terms and phrases to fit a reference does not constitute finding a teaching or suggestion in a reference. Unless the Examiner can point to any teaching, mention, or suggestion of "data points" and "data sets" in Larson, Larson is clearly not a relevant reference.

Next, please consider the second element of claim 1, directed to "considering the data points to be distributed in an n-dimensional data-point space." Again, Larson does not once use the phrases "data points" or "data-point space." Larson is not concerned with data, data sets, or data points.

Next, please consider the third element of claim 1, directed to "determining one or more order-preserving sequences of data points within the *n*-dimensional data-point space." Larson does not once use the phrases "order-preserving sequences," "data points," or "data-point space." Larson does not even use the term "sequence." Larson is concerned with continuous, 3-dimension Cartesian space, and not with sequences. Certainly, sequences can be arbitrarily constructed by selecting points from an illustration. But *Larson* does not do this, and neither teaches, mentions, nor suggests sequences of any kind.

Next, please consider the fourth element of claim 1, directed to "selecting, as normalizing data points, data points from the one or more order-preserving sequences." Larson does not once use the phrases "normalizing data points," "data points," or " order-preserving sequences." Larson does not teach, suggest, or mention anything at all related to data normalization." Larson does not even use the term "normalization."

Next, please consider the fifth element of claim 1, directed to "storing the selected normalizing points in a computer memory as a basis for subsequent normalization of the *n* data sets." Larson does not once use the phrases "normalizing points," "computer memory," or "normalization of the *n* data sets." Larson teaches or suggests nothing related to normalizing data sets.

A simple comparison of the current claim language to Larson's textbook chapter reveals that Larson is completely unrelated to claim 1, or to any other claim in the current application. Again, the Examiner must find these terms, phrases, and concepts in Larson, rather than provide a narrative to Larson's figures unrelated to what Larson clearly states the figures to illustrate, in order to legitimately cite Larson against the current claims that recite these terms, phrases, and concepts.

We next consider several of the Examiner's statements included in the Office Action. On page 5 of the Office Action, the Examiner states:

> The section of Larson et al., entitled, "Solid analytical geometry and vectors in space," describes the method used to normalize data in the instant application.

Larson does not teach any method, or once use the term "method." Larson does not

teach, mention, or suggest anything related to data normalization. Larson basically provides a collection of well-known, simple mathematical formulas and expressions, with graphics to illustrate them, related to Cartesian coordinate spaces and vectors.

The Examiner then attempts to read the claim language, including order-preserving sequences," onto illustrations of: (1) the positive portions of axes in a 3-dimensional coordinate system; (2) an illustration of computing the distance between two points in space using the Pythagorean Theorem; and (3) an illustration of the standard unit-vector notation for a vector. These figures illustrate 3 quite different concepts, none of which is even remotely related to sequences, order-preserving sequences, data points, or any of the other above-noted terms and phrases of the current claims. These illustrations are not described by Larson as having anything to do with data points or sequences. ***Larson*** does not teach, mention, or suggest any of the relevant claim language. Instead, the Examiner is reading claim language, well defined in the current application, and well-understood by anyone even cursorily familiar with computer science or discrete mathematics, on entirely unrelated subject matter. As the Examiner must surely understand, for Larson to be a relevant reference, the Examiner needs to point to teachings ***in Larson***, rather than reinterpret figures in Larson to mean something that Larson clearly does not intend them to mean.

The Examiner states:

> Consequently, two discrete data points in the first octant (0,0,0) and (x,y,z) illustrate an order preserving sequence as part of the rectangular solid illustrated in Figure 14.1 of Larson et al. The vertices connecting the edges of the rectangular solid housing these two vertices are interpreted to be the longest order preserving sequence.

This statement makes no sense mathematically, and has nothing whatsoever to do with the current claim language or current application. Data points have identities and values. The points (0,0,0) and (x,y,z) in 3-dimensional Cartesian coordinate space are merely locations. Their identity is simply a location in 3-diemnsional space. There is no additional value associated with the points. Geometric points do not have sizes, shapes, or any other features or values, apart from their locations. Figure 14.1 does not show a rectangular solid. The statement "[t]he vertices connecting the edges of the rectangular

solid housing these two vertices are interpreted to be the longest order preserving sequence" makes absolutely no sense whatsoever. Were Figure 14.1 to show a rectangular solid, the vertices of the rectangular solid would not constitute a longest order preserving sequence, because there is nothing inherent in a collection of points defining an order, and, as discussed in the previous response, at length, there can be no longest sequence in a continuous solid, because there are an infinite number of points in any line contained within a continuous solid. A straight line connecting two points within a solid represents the shortest path between the two points, not the longest distance. A longer path would be any curve within the continuous solid connecting the two points. While the Examiner seems to feel that, by picking two geometrical points, and defining them to be ordered, the Examiner has therefore discovered an order-preserving sequence - the Examiner's attempts to read the current claims onto an unrelated illustration are of absolutely no relevance to making a *prima facie* case of obviousness. Larson does not select points for a sequence, and does not even use the term "sequence," let alone describe any type of sequence.

In fact, the vertices of a rectangular solid provide a very nice illustration of why Larson does not teach, mention, or suggest anything at all to do with order-preserving sequences. Consider a rectangular solid, of volume equal to 1, with vertices at the Cartesian coordinates (0,0,0), (0, 1, 0), (1, 0, 0), (1, 1, 0), (0,0,1), (0, 1, 1), (1, 0, 1), (1, 1, 1). How would an order-preserving sequence be defined for this collection of points? By adding their coordinates together, and ordering them by the sums? In that case, the computed sums would be 0, 1, 1, 2, 1, 2, 2, and 3, respectively. As is quite apparent, many of the sums are identical, but, as defined in the current application in the above-provided quote, "[a]n order-preserving sequence is a sequence of data points in which the values of the data points within the sequence uniformly increase within the sequence." Thus, the sums of the coordinates would not provide a basis for an order-preserving sequence, because no sequence of the sums can be constructed with a uniform increase in the sums. Another approach might be to order the points by distance from the origin (0, 0, 0). In that case, the points would have distances from the origin of 0, 1, 1, $\sqrt{2}$, 1, $\sqrt{2}$, $\sqrt{2}$, and $\sqrt{3}$. The distance from the origin is also not a basis for an order-

preserving sequence, because 3 vertices have a distance of 1 from the origin, and three other vertices all have a distance of $\sqrt{2}$ from the origin. Most importantly, Larson does not teach, mention, or suggest anything at all related to sequences and order-preserving sequences, and unless the Examiner can point to such a teaching, mention, or suggestion ***in Larson***, then Larson is simply not a suitable reference.

The Examiner states:

Each data point has a value in each of the three dimensions.

As discussed above, Larson does not once mention data points, and is not concerned with data points or data sets. What value is the Examiner postulating for geometric points? The location of a geometric point, in 3-diemsnional space, can be specified by three distances in three different directions, in a rectilinear coordinate system, a pair of angles and distance, in a spherical coordinate system, and by other parameters in other types of coordinate systems. These distances or angle are together sufficient to specify a location of the point, essentially the identity of the geometric point. The geometric point has no value apart from its location or identity. By contrast, a data point has both a value and an identity.

The Examiner states:

The rectangular solid in Figure 14.1 of Larson et al. illustrates a situation where data points are ordered and traversed in the x, y, and z dimensions (each edge of the rectangular solid illustrates such a traversal in each dimension) in order to find greatest metric sums based on changes in each of the three dimensions. Additionally, there are several iterative paths one can take from (0,0,0) to (x,y,z) via varying the order in which the dimensions are traversed.

Applicants' representative can find no hint or suggestion of anything mentioned in this paragraph anywhere in Larson. Figure 14.1 of Larson does not illustrate a rectangular solid and does not illustrate data points. Larson does not teach, mention, or suggest traversals of any kind, and does not once use the word "traversal." Larson does not use the phrases "metric sum" or "greatest metric sum." Applicants' representative cannot find a single occurrence of the phrase "iterative path" in Larson or in the current application or current claims, and has absolutely no idea of what the phrase refers to, or what relationship this phrase might have with anything in the current claims. Larson does not

anywhere mention "order of dimensions." Again, Figure 14.1 of Larson simply shows the positive portion of each coordinate axis in 3-dimensional Cartesian coordinate space, as clearly stated by Larson.

The Examiner states "[t]he last sentence of the article of Schadt et al. emphasizes the use of computing in finding order preserving sequences by stating on page 12:" and then proceeds to quite a paragraph from Schadt that does not use the phrase "order preserving sequences" and that has nothing whatsoever to do with order preserving sequences. As stated in the previous response:

> Of the four cited references, only Schadt is closely related to the subject matter of the current claims. In fact, Schadt is quite relevant. Schadt states, on page 123:
>
> > To address these problems, we have developed an invariant difference selection algorithm (IDS) that chooses a subset of PM/MM intensity differences to serve as the basis for fitting a normalization relation. A set of probes are said to be invariant if the ordering of these probes according to the PM/MM differences in the experiment array, is the same as that in the baseline array.
>
> However, Schadt then states, also on page 123:
>
> > Although the maximal invariant set can be computed using a dynamic programming algorithm (not presented), the resulting set is typically too small to form a reliable normalization curve.
>
> In other words, Schadt rejects the approach disclosed in the current application, and explicitly states that Schadt does not disclose a method for computing such a set. Instead, Schadt uses a simple linear interpolation and difference-threshold technique, expressed in the equations on page 123, to try to approximate an invariant set. The difference metric involves an absolute value, indicating that it is a scalar value, such as a distance, rather than a directional value, and therefore cannot be used to select an order-preserving sequence with respect to rank, since ranks below and above a selected rank reference point would have an identical difference metric computed by Schadt.

In other words, Schadt teaches away from the currently claimed invention.

The second rejection again inappropriately and without rational basis cites Larson and Schadt. Like the first rejection, the second rejection makes absolutely no sense. Applicants' representative offered, in the last response, to provide the Examiner with references to texts on discrete mathematics and computer science to provide a basis

for the Examiner to attempt to understand the current application, although the current application provides very clear definitions and consistent use of the claim terms, provides very detailed examples and graphical illustrations of order preserving sequences and method embodiments of the present invention, clearly defines "data sets, "data points," "normalization," and other such claim terms, and even provides a C++ implementation of an embodiment of the present invention. It is unfair to Applicants to continue to incur delays and expenses in responding to baseless rejections of the current claims. Again, should the Examiner need assistance in understanding the current claims and invention beyond the detailed descriptions, illustrations, and C++ implementation provided in the current application, Applicants' representative can provide such assistance, including references to elementary textbooks. Alternatively, Applicants' representative respectfully urges that this application to be transferred to a quantitative art group, such as an art group that deals with applied mathematics and/or computer science on a regular basis.

In Applicant's representative's opinion, all of the claims remaining in the current application are clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

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